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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,107	11/05/2001	Michael J. Hope	10173-072	7809

7590 08/23/2004

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/992,107	HOPE ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 1-9-04 is acknowledged.

Claims included in the prosecution are 55-84.

Claim Rejections - 35 USC § 112

1. Claims 55-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The terms 'empty aqueous cores' and 'Gaussian distribution' now introduced in claim 55 have no support at the locations in the originally filed specification (pages 7-8 and 17 respectively) pointed out for support by the applicant and therefore, deemed to be new matter.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 55-84 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,139,871. Although the conflicting claims are not identical, they are not patentably distinct from each other because liposome sizes of 100-150 nm recited in the claims of said patent is included in instant 'greater than about 100 nm sizes; instant claims include the specific amounts of phospholipids recited in the claims of said patent.

Applicant argues that this rejection should either be withdrawn because of the amendment or maintained in abeyance. Applicant's amendment will not overcome the rejection since instant composition claims fall within the limits of the generic patented claims and therefore, the rejection is maintained in abeyance as per applicant's request.

In view of the amendments, the 102 rejections are withdrawn.

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 55-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 470 437.

EP teaches unilamellar liposomes having an average diameter of 100 nm containing phosphatidylcholine for the treatment of atherosclerosis (note pages 10, 11, 15 and 16 of the English translation). EP does not provide specific examples for the treatment of atherosclerosis. It would however, been obvious to an artisan to use liposomes for the treatment of atherosclerosis based on the teachings of EP. Although in Example 3 where the liposomes of claimed sizes are prepared, the reference indicates the attachment of a DNA marker to the liposomes, it is deemed obvious to one of ordinary skill in the art not to attach the marker if the desired goal is only to treat atherosclerosis in humans and not for diagnostic purposes since the reference through examples shows how to make the liposomes of different sizes. EP does not also specifically teach instant protocol of administration. In the absence of showing unexpected results, these parameters are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results.

6. Claims 55-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (BBA, 875, pp., 183-194, 1986) in combination with EP cited above.

Williams teaches a method of administration of liposomes and liposomes together with plasma (contains lipoproteins) and the alterations in lipid metabolism and the regression of experimental atherosclerosis as a result of such an administration (note the Materials and Methods section and the discussion). What are lacking in Williams are the teachings of the sizes of liposomes. However, the methodology

disclosed on pages 184 and 185 indicated that sonicated liposomes were passed through a 0.22 microns filter and therefore, it would have been obvious to one of ordinary skill in the art that the liposomes would contain liposomes of instant sizes. Even assuming that the sizes in Williams are different from instant sizes, one of ordinary skill in the art would be motivated to use liposomes larger than 50 nm with a reasonable expectation of success since EP which deals with the treatment of same disease state advocates the use of liposomes of instant sizes.

Applicant's arguments to the above 103 rejections have been fully considered, but are not found to be persuasive. Applicant argues that EP and Williams do not teach a Gaussian distribution wherein at least 68 % of the liposomes have a mean diameter of 125 +30 nm. This argument is not found to be persuasive since first of all, applicant has presented no evidence to indicate that EP has no Gaussian distribution. With regard to "at least 68 % of the liposomes have a mean diameter of 125 +30 nm", as pointed out before, 'at least 68 % indicates that the value can be between 68 and 100 and the reference teaches 129 nm in example 3; applicant has not shown that this value does not fall within the claimed range. With regard to applicant's arguments that the examiner has failed to show where Hager teaches or suggests that the liposomes are effective in promoting cholesterol efflux without causing a substantial increase in LDL or esterified cholesterol levels, the examiner points out that these are composition claims and not method claims and since the reference teaches empty liposomes for atherosclerosis, the burden is upon applicant to show that the liposomes of EP do not perform the same function. With regard to the unexpected results argued, the examiner points out that one

can determine the unexpected nature of the results only when the prior art liposomes are compared with instant liposomes. The examiner once again reminds applicant that these are composition claims and motivation to use them need not be the same as applicant's. Furthermore, the unexpected results argued by applicant are based on LUV 100 whereas instant claims recite sizes of 125+ 30.

7. Claims 55-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (1984 or 1986) in view of Liu.

Williams (1984) teaches the administration of liposomes for treating atherosclerosis, but does not teach the sizes (pages 418-423). This parameter however, if different from instant invention, is deemed to be an obvious parameter manipulated by an artisan to obtain the best possible results. Instant liposome sizes are also deemed to be obvious to one of ordinary skill in the art in view of Liu's teachings that SUVs of about 120 nm have greater circulation time.

Williams (1986) disclose a method of removal of serum cholesterol using liposomes (note the abstract, Introduction, Materials and Methods and Discussion, last paragraph in particular). Although on page 185, col. 1, Williams discloses the use of 0.22 mm filter, he does not specifically teach instant sizes.

Liu teaches that small liposomes (<200 nm) remain in circulation for a longer periods (note page 348, col. 2, Results on page 350, col. 1).

To prepare liposomes of Williams (1984 or 1986) having sizes within the claimed range would have been obvious to one of ordinary skill in the art since liposomes of those sizes are able to survive the circulation system for longer periods (and hence their

enhanced cholesterol removal effect) as taught by Liu. The protocol of administration is deemed to be an obvious parameter manipulated by an artisan.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Williams also does not suggest using a population of liposomes falling within the claimed Gaussian distribution. This argument has been addressed above. Applicant argues that Williams shows an increase in LDL after the administration of SUVs and applicant points out to Fig. 2A of Williams in this regard. A close examination of this figure appear to indicate that even the corresponding controls have the same peak height and therefore, the examiner is unable to determine whether there is a statistically significant difference between values for the controls and the liposomes. Irrespective of this, the rejection is based on the combination and Liu teaches instant sizes and the motivation to use liposomes of instant sizes. The examiner once again points out that instant claims are composition claims and motivation to use liposomes of instant sizes need not be the same as applicant's. Furthermore, the unexpected results argued by applicant are based on LUV 100 whereas instant claims recite sizes of 125+ 30.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

G S Kishore

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK